

Cancers of the ovary

Case numbers and histological types

Ovarian cancer was the 4th most common cancer diagnosed in women in Ireland between 1994 and 2010, with an average of 376 cases diagnosed annually (Table 1). Of these, 55 cases per year, or 15% of all cancers, were categorised as “borderline tumours”, cancers which were, until recently, regarded as invasive but are now recognised as a distinct group, having a low malignant potential.

90% of all ovarian cancers were diagnosed histologically. Approximately one third of both invasive and borderline cancers were serous tumour types. Half of all borderline cancers were mucinous cell types although these represented just 11% of invasive cancers. The classification changes (from ICD-O-2 to ICD-O-3 coding systems)¹ identifying borderline cancers mostly involve serous and mucinous cell types, so it is worth noting that the 44 or so cases of these borderline tumours diagnosed per year would have been counted as invasive cancers in reports using the older ICD-O-2 system.

1 Approximately 40 cases of endometrioid and clear cell tumours combined were registered per year, almost all of which were invasive. Over a quarter of all epithelial tumours were unspecified adenocarcinomas. 14% of borderline tumours were non-epithelial cancer types, compared to just 4% of invasive cancers. The main non-epithelial cancers were germ-cell and gonadal (sex cord-stromal) tumours.

Where records are available of which ovary was affected (73% of all cases), approximately one-third of women had invasive cancers diagnosed simultaneously in both ovaries, a further one-third in the left only and one-third in the right ovary only. Only 10% of borderline cases were diagnosed in both ovaries simultaneously.

Table 1. Annual average numbers of ovarian cancer (% of total) by tumour category and histological type, 1994–2010

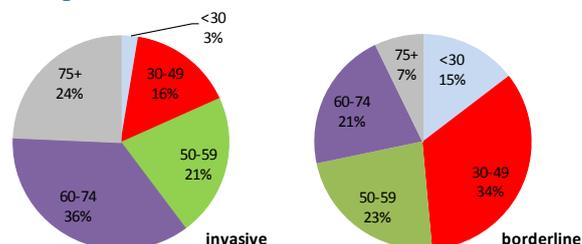
	invasive	borderline
total cases	321	55
histologically diagnosed	281 (88%)	55 (99%)
cancer types: annual average (% of total): histologically confirmed		
serous	97 (35%)	16 (29%)
mucinous	31 (11%)	28 (50%)
endometrioid	25 (9%)	2 (4%)
clear cell	13 (5%)	0 (0%)
other epithelial*	78 (28%)	1 (2%)
germ cell	5 (2%)	2 (4%)
gonadal	3 (1%)	5 (10%)
sarcoma	1 (<1%)	<1 (<1%)
other/unspecified	27 (10%)	1 (2%)

* mostly unspecified adenocarcinomas (93%) with a small number of squamous cell and other cell types

Age profile

Almost one-quarter of all invasive ovarian cancers were diagnosed in women aged 75 or over, over a third in women aged between 60 and 74 and fewer than 20% in women aged under 50 (Figure 1). Borderline ovarian cancers had a younger age profile overall; half of all cases were diagnosed in women aged under 50; 15% of which were recorded in women younger than 30 years. Only 7% of borderline cases were diagnosed in women aged over 75.

Figure 1. Age distribution of ovarian cancers 1994–2010



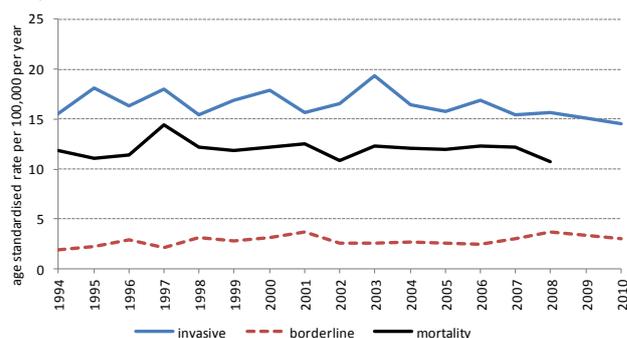
Time trends in incidence and mortality

Age-standardised incidence rates for invasive ovarian cancer ranged from 15 to 19 cases per 100,000 women per year over the 17 year period, 1994–2010 (Figure 2). A slight decline in incidence rates was observed in this period (annual percentage change, APC = -0.7%, 95% confidence interval range (95%CI) = -1.5% to 0.1%). A more pronounced fall in incidence rates was observed from 2003, when a peak of 19.4 cases per 100,000 per year was recorded, to 14.5 cases per 100,000 per year in 2010 (APC = -3.0%, 95%CI = -4.9% to -1.1%).

Between 2 and 4 borderline cases per 100,000 per year were diagnosed between 1994 and 2010 with a slight increase in overall incidence (overall APC= 1.7%, 95%CI = -0.3% to 3.4%).

Mortality rates have remained fairly stable over time, ranging between 11 and 14 deaths per 100,000 women per year - only a slight decline was observed in mortality rates since 1994 (APC= -0.3%, 95%CI= -1.2% to 0.7%). Mortality/incidence ratios have remained relatively constant with between 7 and 8 deaths for every 10 women diagnosed per year.

Figure 2. Trends in ovarian cancer incidence and mortality rates, 1994–2010



Geographical distribution

The incidence of invasive ovarian cancer was highest in the HSE-South and lowest in the HSE Dublin-North East regions, statistically significantly so when compared to overall national incidence rates

(Table 2). A similar pattern of high ovarian cancer incidence in the south of the country has previously been reported.² There was comparatively little difference in incidence rates for borderline cancers between the regions but HSE Dublin & Mid Leinster had the highest incidence (3.4 cases per 100,000 per year).

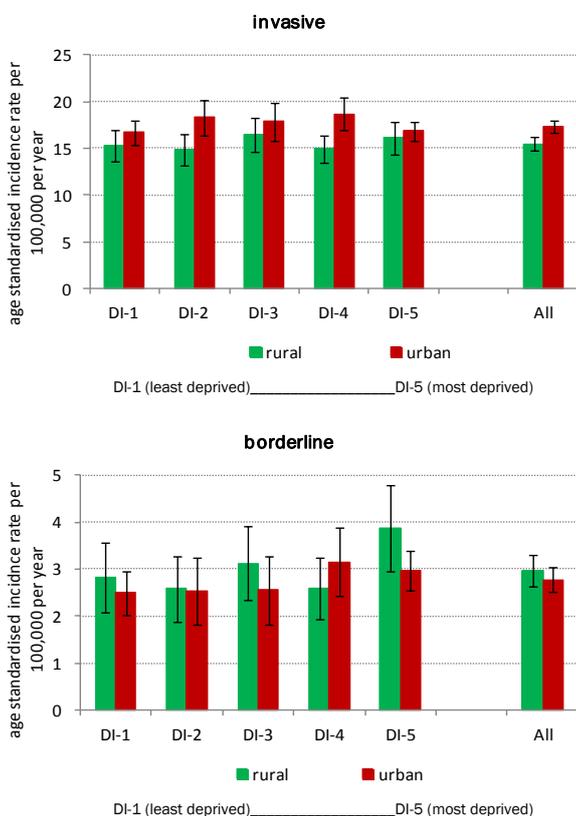
Table 2. Incidence rates (cases per 100,000 per year) (95% confidence interval range) by HSE region, ovarian cancer, 1994–2010

	invasive	borderline
Dublin- Mid Leinster	16.2 (15.4-17.0)	3.4 (3.0-3.8)
Dublin- North East	14.6 (13.7-15.5)	2.6 (2.2-3.0)
South	17.8 (16.9-18.7)	2.6 (2.2-2.9)
West	16.3 (15.4-17.2)	2.6 (2.3-3.0)
Ireland overall	16.3 (15.9-16.8)	2.9 (2.7-3.1)

Relatively little correlation was observed between invasive ovarian cancer incidence and deprivation (Figure 3). Although several lifestyle factors affect a woman’s risk of ovarian cancer, the most important risk factor, family history of disease³, is unlikely to be related to socio-economic status. Therefore it is not surprising that no obvious pattern between incidence and deprivation emerges. Only a faint correlation between incidence and area based socio-economic characteristics for ovarian cancer has previously been reported in Ireland.² Urban areas had higher incidence rates, compared to rural areas, across all deprivation levels. A similar, relatively weak, association with population density in Ireland has previously been reported.²

Borderline cancers of the ovary had generally higher incidence rates in rural compared to urban areas and incidence rates appeared higher in more deprived regions. However this was not statistically significant and likely due to random variation only.

Figure 3. Incidence of ovarian cancer and variation with deprivation index (DI) and urban/rural area of residence, 1994–2009⁴ (DI ranges from 1 (least deprived) to 5 (most deprived)⁵(Rural areas defined by population density <1 person per hectare)

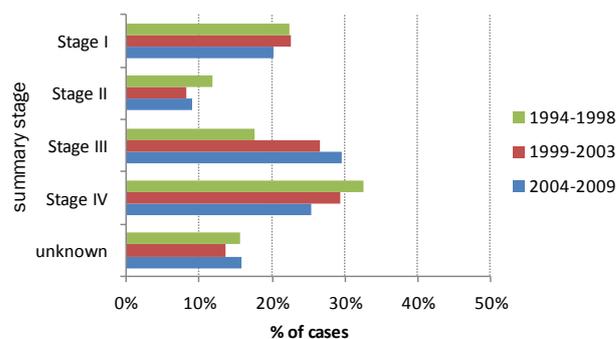


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Stage at diagnosis

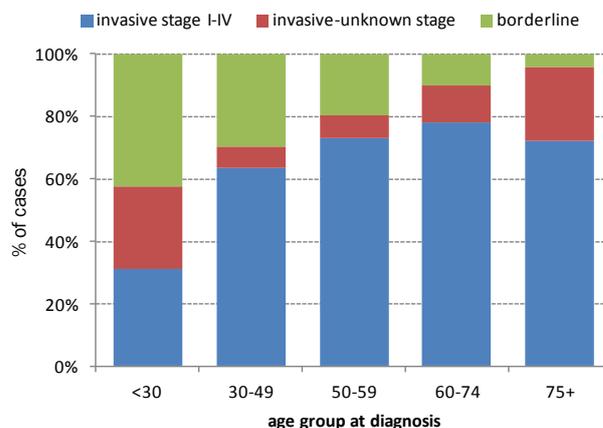
Just over 20% of all invasive ovarian cancers were at stage I, between 9% and 12% were at stage II and 15% were of unknown stage at diagnosis - proportions which have changed little over time (Figure 4). Although a decline in the proportion of patients presenting at stage IV has been observed since 1994-1998, the percentage of women diagnosed at stage III increased from 18% to almost 30% over the same period. Borderline cancers represented between 11% and 16% of all ovarian cancers per year with little obvious change over time.

Figure 4. Percentage of invasive ovarian cancers by stage 1994–2009⁴



The proportion of invasive tumours that were staged, and the proportion of all ovarian cancers that were of borderline malignancy, varied by age group (Figure 5). During 2004-2009, women aged under 30 had the highest proportion of borderline tumours, representing 40% of all ovarian cancers in this group. Almost half of the invasive tumours in the under 30’s were unstaged. This reflects the high proportion of germ-cell tumours in this age group (40% of total) which could not be allocated to summary stage under standard TNM coding. The proportion of unstaged invasive tumours was less than 12% for women aged between 30 and 74. However almost one-quarter of invasive tumours diagnosed in patients aged 75 or over were not staged.

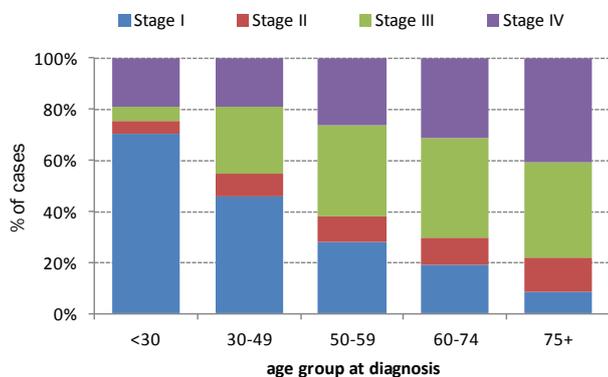
Figure 5. Variation in the proportion of staged invasive and borderline ovarian cancers by age: 2004–2009⁴



Looking in more detail at the distribution of staged invasive tumours by age group (Figure 6), more than 60% of all women aged 50 and over were already at an advanced stage of disease

(stage III-IV) when diagnosed. Almost 20% of the youngest women (aged under 30) were stage IV when diagnosed. The late stage of presentation is largely due to the vague and unspecific nature of early symptoms which often mimic other less serious conditions and are sometimes interpreted by patients as normal changes in the body such as the effects of childbearing, menopause and ageing⁶.

Figure 6. Variation in tumour stage by age group at diagnosis: all staged tumours, 2004–2009⁴

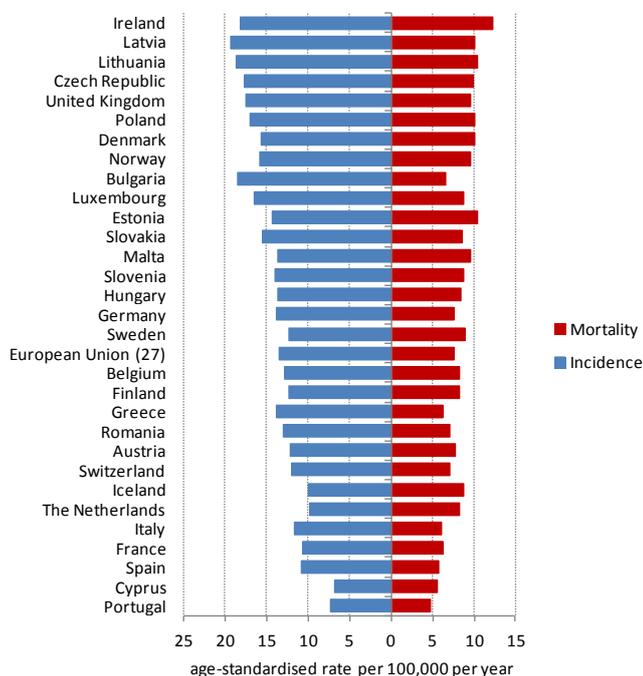


International variation in incidence and mortality⁷

The highest incidence rates for ovarian cancer were recorded in Latvia, Lithuania and Bulgaria, and Ireland ranked 4th highest of 30 countries surveyed (Figure 7). Portugal and Cyprus were ranked lowest with incidence rates of less than 8 cases per 100,000 per year.

Mortality rates ranged from 5 to 12 deaths per 100,000 women per year and Ireland's mortality rate was the highest in Europe. Mortality: incidence ratios were variable ranging from 0.4 in Bulgaria and Greece to 0.8 in Iceland, the Netherlands and Cyprus. Ireland's mortality: incidence ratio in 2008 was 0.7, similar to Malta, Finland, Denmark and Greece.

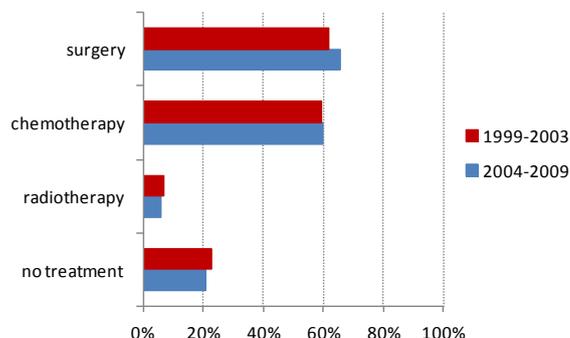
Figure 7. Estimated incidence and mortality for ovarian cancer, 2008⁷



Treatment

There has been little change in the pattern of treatment of patients with invasive ovarian cancer over the 11 year period 1999-2009⁴ (Figure 8). Approximately 60% of patients had tumour-directed surgery and 60% had chemotherapy (half of all patients had both surgery and chemotherapy combined). Less than one in 10 patients had radiotherapy and 20% of all patients had no tumour-directed treatment. Surgery alone was the main treatment for borderline cancers, accounting for 90% of all patients diagnosed.

Figure 8. Treatment by time period: invasive ovarian cancer, 1999–2009⁴



Treatment of invasive cancers varied by stage at diagnosis and age group (Table 3). Almost all patients diagnosed at stage I had tumour-directed surgery, compared to less than half of those patients at stage IV or of unknown stage. 45% of patients with cancers of unknown stage had no tumour directed treatment. Patients staged III or IV were more likely to have chemotherapy than surgery.

The proportion of patients undergoing tumour-directed surgery declined with age; fewer than one-third of patients aged 75 or over had surgery compared to over 90% of those aged under 50. Over half of all patients aged 75 or over had no tumour directed treatment. This may reflect the greater proportion of late stage tumours in older women (Figure 6). 90% of the untreated 75+ year old patients had tumours that were unstaged or late stage (stage III-IV).

Table 3. Percentage of patients treated by tumour stage and age at diagnosis, invasive ovarian cancer, 2004-2009⁴

	surgery	chemo-therapy	no treatment
Tumour stage			
stage I	97%	58%	2%
stage II	70%	64%	19%
stage III	68%	71%	17%
stage IV	48%	65%	26%
unknown	47%	33%	45%
Patient age			
<30 years	91%	56%	4%
30-49 years	92%	68%	3%
50-59 years	84%	76%	5%
60-74 years	69%	70%	14%
75+ years	28%	28%	56%

The type of surgery also varied by stage and age of the patient at diagnosis (Figure 9). The most common procedure overall was bilateral oophorectomy with hysterectomy which represented over 80% of surgical procedures in women with stage II to IV disease. However in patients with stage I disease or of unknown stage,

unilateral oophorectomy without hysterectomy represented approximately one quarter of all procedures. In particular, for women aged under 30 at diagnosis, this represented 80% of all procedures, bilateral oophorectomy making up just 20%. This may reflect a combination of the type of cancer diagnosed in young women (e.g. a high proportion of germ cell tumours which are mostly unilateral⁸) and the need to preserve the possibility of having children after treatment⁹. Other surgery, notably tumour debulking, undertaken to reduce the size of large tumours which can not be completely removed, was the only type of surgery in up to 10% of patients with late stage cancer and in 15% of women aged over 75.

survived for a minimum of 3 years post diagnosis, only one-third of patients aged 60 or over were still alive 3 years after their diagnosis (Table 4).

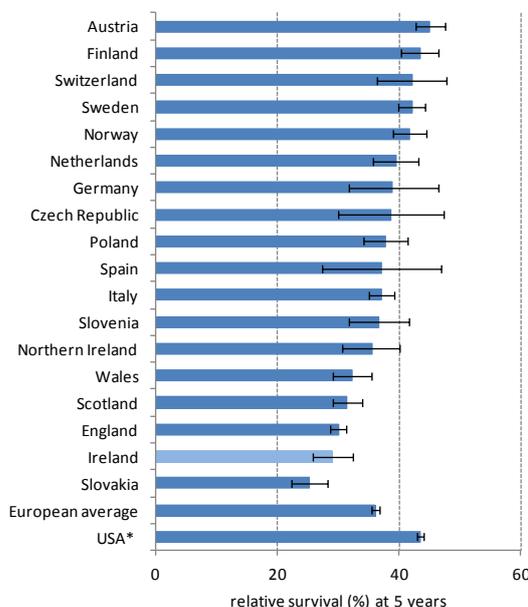
Table 4. Percent of all patients diagnosed with invasive ovarian cancer between 1994 and 2007 that survived a minimum of 3 years post-diagnosis, by age group

<30	30-49	50-59	60-74	75+	All ages
83%	65%	50%	33%	12%	38%

International variation in survival¹¹

Five year relative survival of ovarian cancer patients was 36% in Europe overall for patients diagnosed between 2000 and 2003 and 44% in the US for patients diagnosed 2001-2008 (Figure 9). Ireland (29%) ranked amongst those countries with the poorest survival rates, close to those for England and Scotland but lower than for Northern Ireland. The highest relative survival rates in Europe were found in Scandinavia (Finland, Sweden and Norway) and in Austria and Switzerland.

Figure 9. Five year relative survival for ovarian cancers (period analysis 2000-2003¹¹)

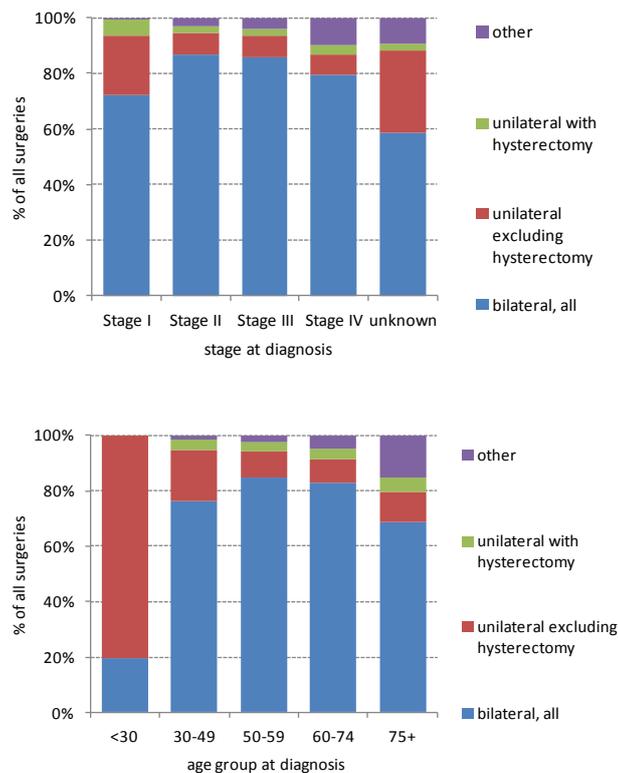


* SEER, 9 registries, 2001-2008

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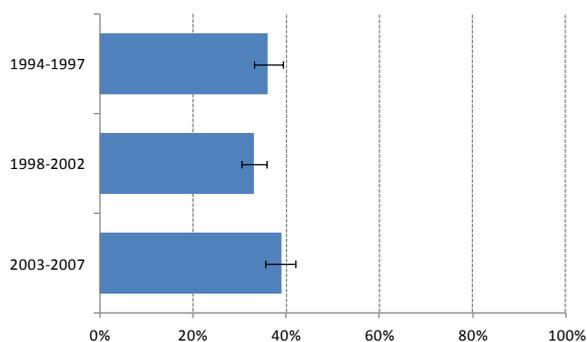
Figure 9. Variation in types of tumour-directed surgery for invasive ovarian cancer by tumour stage and age at diagnosis, 2004-2009⁴



Survival¹⁰

Ovarian cancer survival has changed little in Ireland since 1994-1997, and 5 year survival rates remain poor, at <40% (Figure 8).

Figure 8. Five year relative survival by time period (with 95% confidence intervals) for ovarian cancer¹⁰



Patient survival varies strongly with age, which probably reflects the variation in cancer type, stage and treatment rates between different age groups. Although over 80% of women aged under 30